

## Effects of cumin extract on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, HDL-C, LDL-C, Apo A1, and Apo B in the patients with hypercholesterolemia

Keihan Ghatreh Samani,<sup>(1)</sup> Effat Farrokhi<sup>(2)</sup>

Department of Biochemistry, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran

Email: [ghatreh\\_k@skums.ac.ir](mailto:ghatreh_k@skums.ac.ir)<sup>(1)</sup>

Cellular and Molecular Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

Email: [e\\_farrokhi\\_k@yahoo.com](mailto:e_farrokhi_k@yahoo.com)<sup>(2)</sup>

### Abstract

**Objectives:** Paraoxanase 1 (PON1) plays a protective role against the oxidative modification of plasma lipoproteins and hydrolyzes lipid peroxides in human atherosclerotic lesions. Cumin is the dried seed of the herb *Cuminumcyminum* that is known as *Zeera* in Iran. Cumin seeds contain flavonoids which are now generally recognized to have antioxidant activity and improve the antioxidant system. So, they possibly modify PON1 activity and oxidized low density lipoprotein (oxLDL) level. The present study was aimed to evaluate the effects of cumin extract supplementation on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, High density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), apolipoprotein A1 (Apo A1), and apolipoprotein B (Apo B) in the patients with hypercholesterolemia.

**Methodology:** A fasting venous blood sample was obtained from the voluntary persons before and 45±3 days after taking cumin. Glucose, total cholesterol, and triglycerides were assayed using standard enzymatic procedures. HDL-C and LDL-C were measured by direct method and ApoA1 and ApoB levels by immunoturbidimetric methods. The levels of arylesterase and paraoxanase activities in the samples were measured by photometry methods and oxLDL by enzyme-linked immunosorbent assay (ELISA) method. 3 to 5 drops of cumin extract were added to the patient's diet three times a day based on manufacturer's instruction for 45±3 days. The biochemical parameters were compared before and after taking cumin. Data were analyzed using paired Student's t-test in SPSS statistical software (version 11.5).

**Results:** The results demonstrated that there was a significant decrease in the level of oxLDL after receiving cumin. Paraoxanase and arylesterase activities increased in serum after taking cumin extract.

**Conclusion:** Based on the results, cumin reduces oxLDL level and increases both paraoxanase and arylesterase activity.

**Keywords:** Cuminum, Oxidized low density lipoprotein, High density lipoprotein cholesterol, Paraoxanase 1, Arylesterase, Apolipoprotein A1, Apolipoprotein B

**Abbreviations:** PON1: Paraoxanase 1, oxLDL: Oxidized Low Density Lipoprotein, HDL-C: High Density Lipoprotein Cholesterol, ELISA: Enzyme-Linked Immunosorbent Assay, ApoA1: Apolipoprotein A1, ApoB: Apolipoprotein B, MDA: Malondialdehyde, VLDL: Very Low Density Lipoprotein, IDL: Intermediate Density Lipoprotein, LDL-C: Low Density Lipoprotein Cholesterol, TC: Total Cholesterol, TG: Triglycerides, FBS: Fasting Blood Sugar, BMI: Body Mass Index

### Correspondence:

#### Effat Farrokhi

Cellular and Molecular Research Center,

Faculty of Medicine,

Shahrekord University of Medical Sciences,

Rahmatieh, Shahrekord, Iran;

Tel: +98 381 3346692; Fax: +98 381 3330709

Email: [e\\_farrokhi\\_k@yahoo.com](mailto:e_farrokhi_k@yahoo.com)

## Introduction

Cumin has long been used as a medicinal plant. In diabetic animals, cumin decreases serum glucose levels. It causes bile acid and pancreatic enzymes to secrete in laboratory animals. Cumin oil demonstrated antimicrobial activity in laboratory tests. <sup>(1)</sup> Main constituent and important [aroma compound](#) of cumin is [cuminaldehyde](#) (4-isopropyl benzaldehyde). <sup>(2)</sup> Cumin seeds have flavonoids, which are generally known for their antioxidant activity. <sup>(3)</sup> <sup>(4)</sup> Foods rich in natural antioxidants play an essential role in the prevention of cardiovascular diseases and cancer. Antioxidants are often added to foods to prevent the radical chain reactions of oxidation and to inhibit the initiation and propagation steps, consequently delaying the oxidation process. <sup>(5)</sup>

Cumin has significant inhibitory effects on lipid peroxidation which is measured as formation of malondialdehyde (MDA) production. Significant elevation of the specific activities of superoxide dismutase and catalase was reported in the antioxidant system after cumin taking. <sup>(6)</sup>

Oxidized low density lipoprotein (oxLDL) plays an important role in the development of atherosclerosis. High density lipoprotein (HDL) plays anti atherogenesis and anti coronary heart disease roles. <sup>(7)</sup> HDLs as carriers of enzymes destroy the lipid hydroperoxides that, in turn, contribute to low density lipoprotein (LDL) phospholipids oxidization. Serum concentration of apolipoprotein A1 (ApoA1), which covers the HDL particle, reflects the number of anti atherogenic particles. <sup>(8)</sup> apolipoprotein B (Apo B) is the structural protein of atherogenic lipoproteins, including very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), and LDL. <sup>(9)</sup> Human paraoxanase-1 (PON1) is associated with HDL particles <sup>(10)</sup> and the antioxidant activity of HDL is largely due to the activity of PON1. Previous studies indicated that PON1 played a protective role against the oxidative modification of plasma lipoproteins and hydrolyzed lipid peroxides in human atherosclerotic lesions. <sup>(11, 12)</sup> The present work aims to show the effects of cumin extract supplementation on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, HDL cholesterol (HDL-C), LDL cholesterol (LDL-C), Apo A1, and Apo B in the patients with hypercholesterolemia.

## Materials and Methods

### Patients

This study was conducted from April to August 2010. 39 patients with LDL-C between 100 to 185 mg/dl referred to a clinic of internal medicine in Shahrekord, Iran were enrolled. None of the patients were taking lipid-lowering drugs or any other medication known to affect lipid metabolism before and during the study. The individuals with hypertension, diabetes mellitus, thyroid, hepatic and renal diseases, and smokers were excluded from the study. A consent form was filled out by the patients and the study's whole procedure was approved by the Ethics Committee of Shahrekord University of Medical Sciences (Ethics Code: 87-10-1). 3 to 5 drops of cumin extract (Zardband Pharmaceutical Company, Iran) were added to the patient's diet three times a day based on manufacturer's instruction for 45±3 days.

### Biochemical analysis

A fasting blood sample was obtained from the patients before onset of receiving cumin. The second blood sample was taken 45±3 days after the end of the treatment. Glucose, total cholesterol (TC), and triglycerides (TG) were assayed using standard enzymatic procedures. HDL-C and LDL-C were measured by direct method and ApoA1 and ApoB levels by immunoturbidimetric methods. Creatinine was measured by Jaffe method <sup>(13)</sup> to exclude renal patients. All biochemical tests were measured in serum on BT 3000 automatic analyzer by commercial kits (Pars Azmoon, Iran). Arylesterase activity was measured using phenylacetate as the substrate according to the modified procedure of Kitchen et al. <sup>(14)</sup> PON1 activity toward paraoxon was measured after the reaction of paraoxon hydrolysis into p-nitrophenol and diethylphosphate catalyzed by the enzyme. <sup>(15)</sup> The oxLDL was measured by a sandwich ELISA method using commercial kit (Mercodia-Sweden). The quantitative variables were analyzed using paired Student's t-test (SPSS 11.5) and p value was considered significant when < 0.05.

## Results

All patients fulfilled the process of the study and there were no dropouts. The patients' demographic characteristics are summarized in Table 1.

**Table 1. The patients' demographic characteristics**

Variable	Cumin group (39)
Age	48±10.5
(%)Male	48.7
BMI	25±3.8

The biochemical parameters including Fasting Blood Sugar (FBS), Body Mass Index (BMI), lipid profile, oxLDL, and PON1 enzymes activity were compared before and after taking cumin. Arylesterase activity and paraoxanase

activity were increased by cumin. FBS and oxLDL decreased after cumin taking. Considering other parameters, no significant difference was seen between before and after taking cumin (Table 2).

**Table 2. The biochemical variables before and after receiving cumin**

Variable	Before receiving Cumin	After receiving cumin	P value
BMI <sup>1</sup>	25±3.8	25±3.9	0.33
FBS <sup>2</sup> (mg/dl)	97±15.5	90±10.5	0.04
Total cholesterol (mg/dl)	215±50.5	214±45.6	0.35
Triglycerides (mg/dl)	274±175	259±161	0.21
HDL-C <sup>3</sup> (mg/dl)	45±10.5	42±10.2	0.42
LDL-C <sup>4</sup> (mg/dl)	139±43.3	134±47.5	0.51
ApoA1 <sup>5</sup> (mg/dl)	141±26.6	145±25.5	0.12
ApoB <sup>6</sup> (mg/dl)	116±19.1	117±18.2	0.26
oxLDL <sup>7</sup> (u/L)	85±14.7	76±12.9	0.01
PON1 <sup>8</sup> arylesterase activity	90±32.5	104±38.7	0.04
PON1 paraoxanase activity	185±101	235±143	0.01

1. body mass index; 2. fasting blood sugar; 3. high density lipoprotein cholesterol; 4. low density lipoprotein cholesterol; 5. apolipoprotein A1; 6. apolipoprotein B; 7. oxidized low density lipoprotein; 8. paraoxanase 1.

**Table 3. The biochemical variables before and after receiving cumin**

Variable	Male(n=19)			Female(n=20)			Total(n=39)		
	Before receiving Cumin	After receiving cumin	P value	Before receiving Cumin	After receiving cumin	P value	Before receiving Cumin	After receiving cumin	P value
BMI <sup>1</sup>	26±4.3	25±5.4	0.21	24±3.9	24±5.1	0.41	25±3.8	25±3.9	0.33
FBS <sup>2</sup> (mg/dl)	99±16.5	94±12.7	0.60	88±14.1	80±15.2	0.03	97±15.5	90±10.5	0.04
Total cholesterol (mg/dl)	219±56	221±47	0.39	204±39	199±44	0.55	215±50.5	214±45.6	0.35
Triglycerides(mg/dl)	281 ±195	273±166	0.70	264±161	257±177	0.66	274±175	259±161	0.21
HDL-C <sup>3</sup> (mg/dl)	41±10.5	43±9.8	0.49	49±11.4	45±10.2	0.38	45±10.5	42±10.2	0.42
LDL-C <sup>4</sup> (mg/dl)	141±45.2	140±49.7	0.45	137±41	132 ±46.5	0.43	139±43.3	134±47.5	0.51
ApoA1 <sup>5</sup> (mg/dl)	138±33.3	140±26.4	0.15	149±24.1	152±26	0.18	141±26.6	145±25.5	0.12
ApoB <sup>6</sup> (mg/dl)	123±22	124±18.9	0.31	111±17.5	106±19	0.19	116±19.1	117±18.2	0.26
oxLDL <sup>7</sup> (u/L)	91±15.2	82±13.5	0.02	79±16.1	63±10.5	0.01	85±14.7	76±12.9	0.01
PON1 <sup>8</sup> arylesterase activity	97±28.9	121±41.8	0.02	81±33	96±36.7	0.03	90±32.5	104±38.7	0.04
PON1 paraoxanase activity	187±122.1	245 ±155	0.01	183±77.9	231±93	0.01	185±101	235±143	0.01

1. body mass index; 2. fasting blood sugar; 3. high density lipoprotein cholesterol; 4. low density lipoprotein cholesterol; 5. apolipoprotein A1; 6. apolipoprotein B; 7. oxidized low density lipoprotein; 8. paraoxanase 1.

## Discussion

PON1 activity can be mediated by factors including diet<sup>(16)</sup> and anti oxidant intake. PON1 also was found to be inactivated by oxidized lipids and oxLDL,<sup>(17)</sup> hence oxLDL reduction may lead to increase in PON1 activity that was seen in this study.

PON1 could be a major defense barrier against lipid peroxides. Many studies strongly supported the hypothesis that oxidative modification of LDL contributes greatly to the pathogenesis of atherosclerosis. Arylesterase activity has direct correlation with mass of this enzyme protein<sup>(18)</sup> and serum paraoxanase activity seems most closely related to the inverse relationship with coronary heart disease.<sup>(19)</sup>

Reduction of toxicity of thermally oxidized sunflower's oil was reported in a study on animals following feeding with cumin.<sup>(20)</sup> This protective effect may be due to reduction of oxidized lipids such as oxLDL or activation of some enzymes that have antioxidant property and lead to oxidized lipids destruction.

Reduction of oxLDL in our study may be due to the antioxidant effects of cumin. Cumin is a rich source of flavonoids<sup>(4)</sup> and [cuminaldehyde](#)<sup>(3)</sup> that have been reported as antioxidant substances; therefore, oxLDL level could be decreased by these compounds.<sup>(21)</sup>

Studies on anticancer properties of cumin showed that free radical was scavenged by cumin's materials.<sup>(7, 21)</sup> So, free radical reduction may lead to reduction of oxLDL that was seen in this study.

Manganese and zinc are rich in cumin.<sup>(22)</sup> Manganese can activate superoxide dismutase; an enzyme which destroys superoxide anion protects lipids from oxidation. Cholesterol level did not decrease after cumin extract taking in this study, that is in agreement with a study on animals<sup>(23)</sup> but not consistent with some reports.<sup>(24, 25)</sup>

In this study, we observed that the cumin reduced FBS and could be suggested for diabetes treatment. Cumin seeds could cause hypoglycaemia.<sup>(26)</sup> An aqueous extract of cumin can lower the blood glucose, and plasma and tissue lipids in alloxan diabetic rats.<sup>(25)</sup>

## Conclusion

In this study, cumin reduced oxLDL level and increased PON1 paraoxanase and arylesterase activity.

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